3. Claims 12 stands rejected under 35 U.S.C. § 102(e) as being anticipated by Wu et al. (U.S. Patent No. 6,254,632). Claim 12 has been canceled rendering the rejection moot.

4. Claims 1-9, 11, 12, and 20 stand rejected under 35 U.S.C. § 102(e) as being anticipated by Brown et al. (U.S. Patent No. 6,071,305), or alternatively, under 35 U.S.C. § 103(a) as being unpatentable over Brown et al. alone. Brown et al. teach "a directional drug delivery stent which includes an elongated or tubular member having a cavity containing a biologically active agent." (*see* Abstract). The active agent diffuses from this reservoir cavity "through directional delivery openings arranged on an outer surface of the elongated member." (*see* Abstract). Brown et al, fail to teach or even suggest the use of "**filament portions having a string-like structure** and containing a therapeutic substance disposed in said plurality of grooves" for the delivery of substances. Accordingly, Claim 1 is patentably allowable over Brown et al. Claims 2-9 and 11 depend directly and indirectly from Claim 1 and are patentably allowable for at least the same reason. Claims 12 and 20 have been canceled. Withdrawal of the rejection is respectfully requested.

The Examiner has noted that "if one does not consider the active agent with carrier (23,25) to be fibers, it is the Examiner's position that they are clearly suggestive thereof due to [the] cylindrical elongated structure." The Applicants respectfully disagree with this proposition. Brown et al. lack any suggestion or motivation for the use of string-like filaments in the cavities. The Examiner has failed meet the threshold requirement of *prima facie* obviousness by explaining why cylindrical elongated structures would require string-like filaments. It is the Applicants' position that the mere disclosure of a cylindrical elongated structure does not require or necessitate the use of string-like filament portions. The broad proposition that the use of cylindrical elongated structures clearly suggests the use of filaments is tenuous at best, more

particularly in light of the fact that Brown et al. specifically disclose use of anhydrous and aqueous based solutions, among others, with which to fill the cavities.

Claim 10 stands rejected under 35 U.S.C. § 103(a) as being unpatentable over Brown et al. in view of Fischell et al. (U.S. Patent No. 5,722,984). As indicated above, Claim 1 is patentably allowable over Brown et al. Fischell et al. does not cure the previously described deficiencies of Brown et al. with respect to Claim 1. Accordingly, Claim 1 is patentably allowable over Brown et al. in view of Fischell et al. Claim 10 depends from Claim 1 and is patentably allowable for at least the same reason.

CONCLUSION

Applicant believes pending Claims 1-11 and new claims 21-26 are allowable and allowance of the application is hereby solicited. If the Examiner has any questions or concerns, the Examiner is invited to telephone the undersigned attorney at (415) 954-0200.

Date: 5/10/02

Respectfully submitted,

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Version With Markings To Show Changes Made

In the Specification:

Please amend the title of the invention as follows:

IMPLANTABLE DRUG DELIVERY PROSTHESIS [APPARATUS AND METHOD FOR DELIVERING A THERAPEUTIC SUBSTANCE]

Please amend the paragraph on page 1, line 15 as follows:

Percutaneous transluminal coronary angioplasty (PTCA) is a procedure for treating heart disease. A catheter assembly having a balloon portion is introduced into the cardiovascular system of a patient via the brachial or femoral artery. The catheter assembly is advanced through the coronary vasculature until the balloon portion is positioned across the occlusive lesion. Once in position across the lesion, the balloon is inflated to a predetermined size to radially compress against the atherosclerotic plaque of the lesion [against the inner wall of the artery] to [dilate] remodel the arterial lumen. The balloon is then deflated to a smaller profile to allow the catheter to be withdrawn from the patient's vasculature.

Please amend the paragraph on page 2, line 7 as follows:

A common technique for local delivery of therapeutic substances employs medicated stents. For example, a metallic stent can be coated with a polymeric material which, in turn, is impregnated with a therapeutic substance or a combination of substances. Once the stent is implanted within a cardiovascular system lumen, the drug or drugs are released from the polymer for the treatment of the local tissues. [Disadvantages associated with the aforementioned method include significant loss of the therapeutic substance from the body of the stent during delivery and expansion of the stent and an absolute lack of control of the release rate of the therapeutic

substance from the stent.] What is needed is a stent design with improved mechanical functionality and drug delivery capabilities.

Please amend the paragraph on page 3, line 3 as follows:

In accordance with another aspect of the invention, the grooves can provide a therapeutic material carrying capability for treating intravascular ailments, such as [instent] restenosis and thrombosis. The therapeutic material loading of the grooves can be accomplished in several ways. For example, as described in greater detail below, a pure therapeutic material or a pre-mixed material with a polymer solution, which enhances the adhesion properties of the material, may be deposited directly [in to] into the grooves using conventional spray or modified dip techniques.

Please amend the paragraph on Page 4, line 3 as follows:

FIG. 1 is a simplified perspective view of a [portion of] typical intraluminal prosthesis in accordance with an embodiment of the present invention;

Please amend the paragraph on Page 4, line 10 as follows:

FIG. 4 is a cross sectional view [of a portion of grooves formed into the intraluminal prosthesis of FIGS. 2 and 3] along the line 4-4 of FIG 3;

Please amend the paragraph on Page 4, line 12 as follows:

FIG. 5 is a [simplified illustration of an embodiment of a therapeutic substance loading technique] partial close-up view of a groove loaded with a substance in accordance with one embodiment of the invention;

Please amend the paragraph on page 6, line 4 as follows:

As illustrated in FIG. 2, in one embodiment, stent 20 can include a plurality of [rigid but resiliently flexible] arm elements 22 that are arranged in a [sinusoid-like] configuration that is connected to form a continuous ring or cylinder. The plurality of cylindrical arm elements 22 are radially expandable, disposed coaxially, and interconnected by connecting elements or links 24. Connecting elements 24 are disposed between adjacent cylindrical arm elements 22, leaving gaps or lateral openings 26 between adjacent cylindrical arm elements 22. Although the arm elements 22 are illustratively shown in the form of cylinders or rings connected axially and displaced in-parallel, other configurations, such as helices, coils, or braids, and other connections may be used. Arm elements 22 and connecting elements 24 define a tubular stent body 28 having a lumen contacting surface 30. Lumen contacting surface 30 includes the outwardly exposed surface portions of arm elements 22 and connecting elements 24.

Please amend the paragraph on page 6, line 17 as follows:

FIG. 3 is a close-up view of a portion of stent 20. Arm elements 22 have any suitable width W_1, typically in a range of [widths] width W_1 from about 0.05 mm to about 0.2 mm. A common width W_1 is about 0.08 mm. Connecting elements 24 have any suitable width W_2, typically in a range of [widths] width W_2 from about 0.05 mm to about 0.2 mm. A common width W_2 is about 0.12 mm. Additionally, arm elements 22 and connecting elements 24 have any suitable thickness, typically a thickness in a range from about 0.05 mm to about 0.2 mm. A common thickness T (FIG. 4) is about 0.12 mm. A specific choice of width and thickness depends on the anatomy and size of the target lumen. Thus, the size of the stent can vary

according to intended procedure, anatomy, and usage.

Please amend the paragraph on page 7, line 19 as follows:

The location or placement of grooves 32 on arm elements 22 and connecting elements 24 can vary according to the intended usage and application of stent 20. In one example, grooves 32 are evenly distributed over body [structure] 28 and have an equal volume so that the tissue in contact with stent 20 receives an equal distribution of a therapeutic substance.

Please amend the paragraph on page 7, line 24 as follows:

Grooves 32 can be formed to any suitable open-ended geometrical configuration, for example, a rectangular channel, which can have any preselected depth and size. As illustrated in FIG. 4, depth D_1 of groove 32 can be varied in proportion to the thickness T of connecting element 24 or arm element 22 depending on the clinical purpose and usage. In one embodiment, a suitable groove or channel depth D_1 has a range from about 10% to about [90 %] 90% of thickness T. Typically, a depth not greater than about 50% of thickness T is most suitable. The specific depth D_1 of groove 32 depends on the amount of therapeutic substance that is to be deposited. In one example of stent 20 carrying a radioactive isotope, depth D_1 is typically about 10% to about 80% of thickness T. A more specific suitable depth is not greater than about 30% of thickness T. In another example, stent 20 carrying a radiopaque material, a suitable groove or channel 32 depth D_1 has a range from about 10% to about 90% of thickness T. Typically, a depth not greater than about 65% is most suitable. The upper limit of depth D_1 varies depending on the material characteristics, such as the hardness of the structural material used in stent 20.

Please amend the paragraph on page 8, line 21 as follows:

Referring again to FIG. 3, grooves 32 are substantially aligned in axially displaced rows of grooves 32, where each row extends across stent 20 nearly perpendicular to axis 34. In one embodiment, for a given width W_1 or W_2, the depth D_1 and breadth D_2 (*i.e.*, the volume) of each groove 32 in a row of grooves 32 on stent 20 can vary relative to [each] other [groove] grooves in [each] other [row] rows of grooves 32. In one example, the manufacturer selectively controls the volume of grooves in a row on different positions of body [structure] 28, either selectively varying the volume between rows or making the volume consistent throughout body [structure] 28. For some applications, consistent groove volume provides evenly distributed therapeutic material delivery throughout stent 20 and results in consistent application of the therapeutic substance to the tissues in contact with surface 30 of stent 20.

Please amend the paragraph on page 9, line 3 as follows:

In some embodiments, the therapeutic substance or agent, can include antineoplastics, anti-inflammatory substances, antiplatelets, anticoagulants, [fribrinolytics] fibrinolytics, thrombin inhibitors, antimitotics, and antiproliferatives. Examples of antineoplastics include paclitaxel and docetaxel. Examples of antiplatelets, anticoagulants, [fribrinolytics] fibrinolytics, and thrombin inhibitors include sodium heparin, low molecular weight heparin, hirudin, argatroban, forskolin, vapiprost, prostacyclin and prostacyclin analogues, dextran, D-phe-pro-arg-chloromethylketone (synthetic antithrombin), dipyridamole, glycoprotein IIb/IIIa platelet membrane receptor antibody, recombinant hirudin, thrombin inhibitor (available from Biogen), and 7E-3B® (an antiplatelet drug from Centocore). Examples of suitable antimitotic agents include methotrexate, azathioprine, vincristine, vinblastine, flurouracil, adriamycin, mutamycin and actinomycin D. Examples of suitable cytostatic or antiproliferative agents

include angiopeptin (a somatostatin analogue from Ibsen), angiotensin converting enzyme inhibitors such as Captopril® (available from Squibb), Cilazapril® (available from Hofman-LaRoche), or Lisinopril® (available from Merck); calcium channel blockers (such as Nifedipine), colchicine, fibroblast growth factor (FGF) antagonists, fish oil (omega 3-fatty acid), histamine antagonist, Lovastatin® (an inhibitor of HMG-CoA reductase, a cholesterol lowering drug from Merck), monoclonal antibodies (such as PDGF receptors), nitroprusside, phosphodiesterase inhibitors, prostaglandin inhibitor (available form Glazo), Seramin (a PDGF antagonist), serotonin blockers, steroids, thioprotease inhibitors, triazolopyrimidine (a PDGF antagonist), and nitric oxide. Other therapeutic substances or agents which may be appropriate include alphainterferon, genetically engineered epithelial cells, and dexamethasone.

Please amend the paragraph on page 12, line 1 as follows:

In one embodiment, stent 20 can be coated with a therapeutic substance in addition to having a therapeutic substance deposited in channels 32. The therapeutic substance is a substance that is capable of absorbing or attaching to the prosthesis surface. For example, highly suitable therapeutic substances for a stainless steel prosthesis include paclitaxel and dexamethasone, substances that easily attach to a metallic substrate.

Please amend the paragraph on page 13, line 3 as follows:

[Biomolecules such as heparin, fibrin, fibrinogen, cellulose, starch, and collagen represent can be used to coat, or alternatively, can be embedded into the polymer.]

In the Claims:

Please amend Claims 1 and 9 as follows. The italicized claims have not been amended and are provided for the Examiner's convenience.

1. (Amended) An implantable prosthesis, comprising:

a body structure having an outer surface [capable of] for contacting a surface of a vascular lumen;

a plurality of grooves [defined] disposed on said outer surface of said body structure; and

filament portions having a string-like structure and containing a therapeutic substance disposed in said plurality of grooves.

2. The implantable prosthesis of Claim 1, wherein each of said plurality of grooves has a preselected and controlled distribution and a preselected and controlled depth.

3. The implantable prosthesis of Claim 2, wherein said preselected and controlled depth is equal to about 10% to 90% of a thickness of said body structure.

4. The implantable prosthesis of Claim 2, wherein said preselected and controlled depth is not greater than about 65% of a thickness of said body structure.

5. The implantable prosthesis of Claim 1, wherein each of said plurality of grooves are open ended.

6. The implantable prosthesis of Claim 1, wherein said plurality of grooves are formed by exposing said outer surface to an energy discharge from a laser.

7. The implantable prosthesis of Claim 1, wherein each of said plurality of grooves are formed in rows extending approximately perpendicular to a central longitudinal axis of said body structure.

8. The implantable prosthesis of Claim 1, wherein each of said filament portions comprise a polymer material.

9. (Amended) The implantable prosthesis of Claim 1, wherein said therapeutic substance comprises a substance selected from the group consisting of antineoplastic, antiplatelet, anticoagulant, [fribrinolytics] fibrinolytic, antimitotic, thrombin inhibitor, antiinflammatory, and antiproliferative agents.

10. The implantable prosthesis of Claim 1, wherein said therapeutic substance comprises a radioactive isotope.

11. The implantable prosthesis of Claim 1, further comprising a barrier formed on said outer surface of said body structure, wherein said barrier covers each of said plurality of grooves to reduce the rate at which said therapeutic substance is released.

Please cancel claims 12-20 without prejudice.

Please add the following new claims:

--21. The implantable prosthesis of Claim 1, wherein said body structure is a radially expandable tubular structure.

22. The implantable prosthesis of Claim 1, wherein said body structure includes arm elements joined by connected elements.

23. The implantable prosthesis of Claim 1, additionally including an adhesive bonding said string-like filament portions in said grooves.

24. The implantable prosthesis of Claim 1, wherein the thickness of said string-like filament portions is generally equivalent to the width of said grooves so as to provide a tight fit between said string-like filament portions and said grooves.

25. The implantable prosthesis of Claim 1, wherein the thickness of said string-like filament portions is generally equivalent to the depth of said grooves such that said string-like filament portions do not protrude out from said grooves.

26. A stent comprising

a radially expandable body, a first channel located in one section of the outer surface of the radially expandable body, and a second channel located in another section of the outer surface of the radially expandable body, wherein the volume of the first chamber is larger than the volume of the second chamber.--